



Epidemiological Aspects of the Carotid Artery Disease in Patients Undergoing Coronary Artery Bypass Grafting: A Cross-sectional Study

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Abstract

Background and aims: Concomitant carotid artery disease (CaAD) in patients referred to coronary surgical revascularization is a strong hazard to perioperative stroke. The current study addressed the epidemiology features of concomitant CaAD in patients referred to a coronary surgical revascularization center.

Methods: This descriptive-analytical cross-sectional study was conducted on all incoming patients to coronary surgical revascularization for two years at a single center who underwent a color duplex-sonography (CDS) interrogation. The demographic, clinical, echocardiographic, coronary angiographic, and color duplex-sonographic data were collected from patients' medical records. Quantitative and qualitative data were expressed as means and standard deviations, as well as numbers and percentages, respectively. The relationships between quantitative and qualitative variables were investigated using Pearson's correlation and chi-square test, respectively.

Results: In total, 430 patients with a mean age of 66.3 ± 9.9 years were included (35% females) in the study. Preoperative CDS was performed on 82% of patients; in addition, 29% of them presented with an increased intima-media ratio, and CtAD was observed in 51%. Based on the results, 77 and 143 patients were detected with unilateral and bilateral involvement, respectively. Severe carotid stenosis accounted for 4% of patients. Age older than 65 years ($P=0.02$), unstable angina ($P=0.045$), and the presence of an occluded coronary artery ($P=0.002$) were associated with the presence of CtAD. Finally, the severity of the left and right carotid stenosis was associated with diabetes mellitus ($P<0.05$).

Conclusion: The prevalence of concomitant CtAD in patients referred to coronary surgical revascularization remains high. The current data warn of the necessity of performing preoperative CDS routinely.

Keywords: Carotid artery, Atherosclerosis, Stroke, Coronary artery bypass grafting, Color duplex-sonography

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Introduction

Coronary artery bypass grafting (CABG), also called heart bypass surgery, is a medical technique to improve blood flow to the heart. It may be needed when the arteries supplying blood to the heart, called coronary arteries, are narrowed or blocked.¹ With about 400 000 operations performed each year in the United States, CABG is one of the most frequently performed major surgical procedures.² CABG remains a valid revascularization method, especially for those patients unsuitable for percutaneous coronary intervention (PCI).³ CABG faces more complex patients with advanced atherosclerotic disease that could raise the hazards of arterial involvement

rather than coronary artery branches. The principal aim of CABG by the perioperative time is not only to ensure myocardial protection, but also to prompt organ protection, including structural and functional integrity of the brain, kidneys, and lungs.⁴ Perioperative stroke is a major adverse cardiovascular event that seriously jeopardizes CABG benefits.⁴⁻⁶ Continuous efforts have been paid to minder the incidence of perioperative stroke by better recognizing the underlying risks of stroke. Avoiding manipulating an atherosclerotic aorta (Untouched aortic surgery), careful policy to blood transfusion, and use of pulsatile flow during the CABG procedure constitute some of the compelled progress in

perioperative brain protection. The carotid disease has been implicated as a major factor, leading to an increased risk of perioperative stroke by the time of CABG.⁵ Peri-procedural hemodynamic perturbations in association with dysregulation in haemato-encephalic blood barrier integrity and an increase in central venous pressures do predispose any carotid artery critical stenosis, leading to cerebral hypoperfusion. Therefore, seeking more secure perioperative brain organ protection should reasonably incite to detect any critical concomitant carotid artery disease (CaAD). Screening is routinely and perioperatively performed by many cardiac surgical teams in order to find out the associated atherosclerotic of the neck arterial axes.^{4,7,8} Nevertheless, the rationality of the latter approach has yet not gained wide acceptance and remains a theoretical clinical realm.⁹⁻¹¹ The results of studies conducted in this field are somewhat different in various regions of the world. The heterogeneity in the results of reported studies is sourced by the ethical difference, various nutritive regimens, the disparity in resorting the cardiovascular primary and secondary prevention programs across the countries and regions, the dissimilar accessibility to health resources, and the cultural variances to adherence of health recommendations.^{12,13} For better apprehending clinical and therapeutic implications and defining national management guidelines with the aim of increasing patient safety and cost-effectiveness of programs, it is advised to undertake regular and continuous evaluations of the epidemiologic features of patients with concomitant CaAD who are referred to CABG. Accordingly, the current study was designed to investigate the epidemiological aspects of CaAD and its association with the demographic, medical history, and coronary angiographic data in patients referred to CABG in Chaharmahal and Bakhtiari province, in Iran.

Materials and Methods

Study Design and Study Population

The current descriptive-analytical cross-sectional study was conducted in the Ayatollah Kashani hospital, the largest university hospital in Shahrekord (the capital city of Chaharmahal and Bakhtiari province, in Iran). This study included all patients who underwent CABG from 2017 to 2019.

Information Source and Data Collection Tool

The medical records of patients were reviewed, and different data were extracted and collected, including demographic data, past medical history, patients' habits (smoking, addiction, and alcoholism), the clinical presentation (elective, urgent, and emergent), and the percentage of left ventricle systolic ejection fraction determined by echocardiography. Data related to metabolic risk factors determined by blood analysis (cholesterol, triglyceride, thyroid hormones, and blood sugar), the results of coronary angiography with regard to coronary stenosis severity and occlusion, and the type

of coronary artery disease (CAD) were obtained as well. Finally, the other collected data were associated with the morphologic and functional results afforded by the color duplex-sonography (CDS) interrogation of the neck arterial axes (carotids and vertebral arteries).

Eligibility Criteria

Patients undergoing CABG with concomitant procedures were excluded from this study. The color sonography of the neck arterial axes was performed either preoperatively or postoperatively.

Statistical Analysis

Quantitative and quantitative data were expressed as means \pm standard deviations (SD), as well as numbers and percentages, respectively. The relationships between quantitative and qualitative variables were evaluated by Pearson's correlation and chi-square test, respectively. Further, the t-test was used to investigate the difference in the mean of quantitative variables. All analyzes were performed by SPSS statistical software (version 26), and the significance level was considered < 0.05 .

Results

Demographic and Past Medical History

In total, 430 patients with a mean age of 66.3 ± 9.9 years (31-91) were enrolled in the current study, of whom 219 (51%) patients were older than 65 years, and 150 (35%) of them were females. The average age of the females and males was 66.6 ± 10 (42-92) and 66.1 ± 10 (31-89) years, respectively; this difference was statistically significant ($P < 0.001$).

A history of cerebrovascular adverse events was observed in 35 (8%) patients so that 10 (2.3%) patients had prior transient ischemic accidents, and the remaining 25 (6%) cases had cerebrovascular accidents. Additionally, a history of surgical carotid artery endarterectomy was observed in 1 patient, and percutaneous carotid intervention was found in 2 patients. Previous myocardial infarction (MI) was detected in 97 (23%) patients, and in 78 (18%) patients, it was observed within the preceding 90 days; the results demonstrated that 22 (5%) patients had a PCI, and 10 (2.3%) patients underwent previous CABG. Eventually, a concomitant heart valvopathy was present in 148 (34%) patients (Table 1).

Clinical Presentation

In the current series, 383 (90%) of patients referred to CABG contracted an acute coronary syndrome (ACS). Unstable angina was the most prevalent clinical status in 254 (59%) patients, followed by ST-segment elevation myocardial infarction (STEMI) and non-ST segment elevation MI (NSTEMI) in 104 (24%) and 25 (6%) patients, respectively. Coronary angiography was performed as elective, urgent, and emergent procedures in 187 (43%), 146 (34%), and 100 (23%) patients, respectively. Concomitant cerebrovascular accident related to ACS occurred in 14 (3%) of the patients

(Table 2). The mean systolic ejection fraction of the left ventricle was $43 \pm 10\%$.

A left main (LM) disease and an LM three-vessel disease were diagnosed in 8 (2%) and 74 (17%) patients, respectively, and a three-vessel disease was found in 232 (54%) patients. One or more occluded coronary artery or depending branches was present in 180 (42%) patients. An

arterial occlusion of the left anterior descending (LAD) artery system was depicted in 89 (21%) patients. An arterial occlusion on the left circumflex coronary (LCx) artery and the right coronary artery (RCA) was noticed in 72 (16.5%) and 75 (17%) patients, respectively. A proximal disease in LAD, LCx, and RCA was found in 273 (63%), 214 (50%), and 206 (48%) patients, respectively (Table 3).

Table 1. Patients' Demography and Past Medical History

| Study Variables | No. (%) |
|--|----------|
| Gender | |
| Female | 150 (35) |
| Male | 280 (65) |
| Active smoker | 43 (10) |
| Hypothyroidism | 14 (3.3) |
| Hypercholesterolemia | 152 (35) |
| Hypertriglyceridemia | 152 (35) |
| Diabetes mellitus | 116 (27) |
| Insulin therapy | 59 (14) |
| Oral hypoglycemic therapy | 48 (11) |
| Chronic obstructive pulmonary disease | 47 (11) |
| Chronic dialysis | 20 (5) |
| Prior cerebrovascular events | 35 (8.2) |
| Transient ischemic attack | 10 (10) |
| Cerebrovascular accident | 25 (6) |
| Prior carotid surgical endarterectomy | 1(0.23) |
| Prior carotid artery intervention | 1(0.23) |
| Previous myocardial infarction | 97 (23) |
| Myocardial infarction <90 days | 78 (18) |
| Concomitant heart valve disease | 148 (34) |
| Prior percutaneous coronary intervention | 22 (5) |
| Previous coronary artery bypass grafting | 10 (2.3) |
| Peripheral vascular disease | 2 (0.5) |
| ASA | 264 (61) |
| Statin | 392 (91) |
| Beta-blockers | 283 (63) |
| Angiotensin-converting enzyme inhibitors | 161 (37) |
| Clopidogrel | 158 (37) |

Note. ASA, acetylsalicylic acid.

Table 2. Clinical Status of the Carotid Artery Disease in Patients Undergoing Coronary Artery Bypass Grafting

| Variable | No. (%) |
|---|----------|
| Acute coronary syndrome | 383 (90) |
| Unstable angina | 254 (59) |
| T-segment elevation myocardial infarction | 104 (24) |
| Non-ST-elevation myocardial infarction | 25 (6) |
| Coronary angiography | |
| Elective | 187 (43) |
| Urgent | 146 (34) |
| Emergent | 100 (23) |
| Concomitant cerebrovascular accident | 14 (3) |

Neck Vessels Colour-duplex Sonography Interrogation

The CDS interrogation of carotid and vertebral arteries was performed preoperatively in 351 (82%) patients prior to CABG; the remaining interrogation was performed after the surgical procedure. Requesting pre-CABG CDS was statistically associated with the ACS ($P=0.009$) and the presence of coronary artery occlusion ($P=0.034$), while the severity of LM disease, the presence of proximal CAD in any of the three major coronary arteries, nor the CAD type was not associated with the prevalence of requesting pre-CABG neck vessel CDS screening ($P>0.05$).

Vertebral Arteries

A hemodynamically significant stenosis or an arterial occlusion in the right vertebral artery was depicted in 6 (1.5%), and 4 (1%) patients, respectively. A hemodynamic stenosis in the left vertebral artery was found in 4 (1%) patients. Therefore, 14 (3.5%) patients displayed critical perfusion of at least one vertebral artery axes.

Carotid Arteries

An increase in carotid intima-media thickness (IMT) was noticed in 125 (29%) patients; the prevalence of IMT was statistically more in patients with age >65 years old ($P=0.012$), while the patient gender did not influence the latter ($P=0.16$). IMT detection was associated with the presence of an occluded LAD ($P=0.025$), RCA ($P=0.001$), unstable angina ($P=0.005$), and CABG status

Table 3. Coronary Angiographic Data of Patients Undergoing Coronary Artery Bypass Grafting

| Variable | No. (%) |
|--------------------------|-----------|
| LM disease | 8 (2) |
| LM 3VD | 74 (17) |
| 3VD | 232 (54) |
| Occluded coronary artery | 180 (42) |
| LM occlusion | 5 (1.4) |
| LAD occlusion | 89 (21) |
| LCx occlusion | 72 (16.5) |
| RCA occlusion | 75 (17) |
| PDA occlusion | 10 (2.4) |
| LM disease | 211 (49) |
| LAD proximal disease | 273 (63) |
| LCx proximal disease | 214 (50) |
| RCA proximal disease | 206 (48) |

Note. LM: Left main coronary artery; LCx: Left circumflex artery; PDA: Posterior descending artery; RCA: Right coronary artery; VD: Vessel disease; LAD: Left anterior descending artery.

($P=0.008$). Among the investigated metabolic risk factors, hypothyroidism demonstrated an association with IMT presence ($P=0.038$).

Overall, the rate of an abnormal blood flow pattern in the left and right carotid arteries was estimated as being 8.4 % (36 patients) and 7% (30 patients), respectively. There was a statistically significant association between the patient's age >65 years old with the prevalence of represented CtAD ($P=0.02$). On the contrary, the patient's gender was devoid of any statistically significant association with the CtAD prevalence ($P=0.10$). CaAD and bilateral were diagnosed as being unilateral in 77 (18%) and 143 (33%) patients, respectively, accounting for a total percentage of CaAD prevalence of 51% to the current series of patients referred to CABG.

The presence of an occluded coronary artery was associated with bilateral CtAD ($P=0.002$). The investigated metabolic risk factors (diabetes mellitus [DM], hypercholesteremia, hypertriglyceridemia, and hypothyroidism) and the intake of primary or secondary cardiovascular prevention drugs (Acetylsalicylic acid [ASA], statin, beta-blocker, and ACEIs) were not associated with the prevalence of CtADs ($P>0.05$). There was a trend toward an association between peripheral vascular disease and CtADs but not reaching statistical significance ($P=0.05$).

Left Carotid Artery

Prevalence of Left Carotid Artery Disease

LtCA disease accounted for 54% of all CtADs among the patients who were referred to CABG. There was a significant association between the age >65 years old and the prevalence of LtCA disease ($P=0.002$). The LtCA disease prevalence was related to the presence of coronary occlusion ($P=0.01$); among the major epicardial arteries, only the proximal stenosis of LCx demonstrated a significant association with the prevalence of LtCA disease ($P=0.03$); nonetheless, the unstable angina was associated with the presence of LtCA disease ($P=0.02$).

Severity of Left Carotid Artery

There was neither any association between the patient age >65 years old and the severity of the LtCA stenosis ($P=0.054$). Among 197 (46%) patients affected by LtCA disease, 120 (28%) cases displayed a hemodynamic stenosis estimated as mild, moderate, and severe in 73 (60%), 41 (34%), and 6 (1.4%) patients, respectively. The patient's gender did not affect arterial stenosis severity ($P=0.100$). The severity of LtCA stenosis was associated with LAD occlusion ($P=0.013$) and LCx proximal segment stenosis ($P=0.025$). Among the investigated metabolic risk factors, only DM was strongly related to the severity of LtCA stenosis ($P<0.001$).

Right Carotid Artery

Prevalence of Right Carotid Artery Disease

There was a statistically significant association between

the patient's age >65 years old with the prevalence of RCA disease ($P=0.012$) and the prevalence of abnormal arterial blood flow on duplex interrogation ($P=0.012$).

The presence of an occluded coronary artery was strongly associated with the prevalence of RtCA disease ($P=0.009$), as well as LAD occlusion ($P=0.017$). Among the evaluated metabolic risk factors, only hypothyroidism was related to the prevalence of RtCA disease ($P=0.011$).

Severity of RtCA Stenosis

Among 193 (45%) patients affected by the right carotid disease, 108 patients displayed a hemodynamic stenosis, including mild, moderate, and severe stenosis in 67 (62%), 30 (28%), and 11 (10%) patients, respectively. The patients' age >65 years old was associated with the prevalence of RtCA disease ($P=0.010$).

When accounting for the possible association between CAD features and the severity of CA stenosis; the LM coronary artery occlusion ($P=0.56$), the severity of LM stenosis ($P=0.62$), LAD occlusion ($P=0.059$), RCA occlusion ($P=0.18$), and LCx occlusion ($P=0.15$) were not associated with the severity of CA stenosis. Likewise, the presence of proximal arterial disease in any of the three major coronary arteries ($P>0.05$), and the CAD type ($P=0.28$) were not related to the CA stenosis severity. The type of ACS ($P=0.67$) and the CABG status ($P=0.42$) were not related to the severity of RtCA.

Of notice, there was no association between the intake of primary or secondary cardiovascular prevention drugs such as ASA ($P=0.290$), statin therapy ($P=0.132$), beta-blockers (0.180), angiotensin converter or receptors inhibitors ($P=0.32$), and the severity of RtCA stenosis.

Discussion

The current study was designed to investigate the epidemiological aspects of CaAD and its association with demographic, medical history, and coronary angiographic data in patients referred to CABG. In this study, 430 patients with a mean age of 66.3 ± 9.9 years were enrolled, of whom 51% were older than 65 years, and 35% were females. A history of cerebrovascular adverse events and MI was observed in 8% and 23% of patients, respectively. In the current series, 90% of the patients referred to CABG followed an ACS. Unstable angina was the most prevalent clinical status (59%) of patients, followed by STEMI (24%) and NSTEMI (6%). The neck arterial axa CDS was performed in 82% prior to CABG; there was a significant statistical relationship between the ACS and the presence of any occluded coronary artery with requesting CDS prior to CABG. The increase in the IMT ratio was present in 125 patients (29%) and was associated with an age older than 65 years old, unstable angina, urgent CABG status, occlusion of LAD, occlusion of RCA, and the presence of hypothyroidism.

The coexistence of concomitant atherosclerotic involvement of the neck arterial axes in patients referred to CABG is advocated as a source of perioperative

stroke.¹² Severe stenosis or stenosis with a jeopardizing morphology may change the strategy that should adopt before proceeding with CABG, including prior carotid intervention, prior surgical carotid endarterectomy to CABG, or planning a concomitant carotid artery endarterectomy by the time of CABG.^{12,14} The prevalence of CaAD may vary among different populations which may explain contradictory reported results.^{5,12,14-16} On the other hand, the population's access to health care and primary and secondary prevention programs has changed the epidemiologic aspects of this vascular atherosclerotic association between CAD and CtAD in the past decades. The latter features do differ in CAD patients and those CAD patients referred to CABG¹⁶; inciting separate digging into related risk factors to CtAD in CABG patients. Additionally, the adoption of the off-pump beating heart CABG approach has set the classical management and therapeutic algorithms up in the face of associated CtAD to patients referred to CABG, and in comparison, to the on-pump CABG approach. Therefore, it seems logical and mandatory that the local guidelines for cost-effectively managing the associated CtAD in terms of diagnosing and treating are being developed for patients referred for CABG.

In a study conducted by Sahadevan et al on more than 100 CABG patients, it was observed that 56.3% of patients had an increased IMT ratio, and an age older than 66 years was associated with the presence of carotid plaques.¹³

In this study, CtAD, unilateral, and bilateral were detected in 220 (51%) patients candidates for CABG, and 77 (18%) and 143 (33%) patients, respectively. In their study on 200 patients referred to CABG, Adhikary et al found that bilateral CtAD was associated with the severity of CtAD.¹² Age older than 65 years old, unstable angina, and the presence of an occluded coronary artery were associated with the presence of CtAD. Contrary to Tanimoto et al, reporting a statistical association between the CAD severity and the prevalence of CtAD,¹⁶ the findings of the current study represented no relationship between the prevalence of CtAD and the CAD severity or the disease of the proximal segments of the major epicardial arteries in CABG patients. Many studies reported a statistical association between cardiovascular metabolic risk factors (e.g., DM and dyslipidemia) and the CtAD prevalence^{5,12,14}; the current study failed to demonstrate any association between the investigated metabolic risk factors and the prevalence of CtAD, reflecting the efficacy of cardiovascular prevention therapies as 91% of the patients were under statin therapy, and 25% of 27% of patients affected by DM were treated chronically. The association of old age with the prevalence of CtAD in patients suffering from CAD or referred to CABG was reported in nearly all reported studies; highlighting the ongoing inefficacy of cardiovascular prevention therapy on the vascular aging process.^{10,13,16} The prevalence of CtAD was 45% and 46% for RtCA and LtCA, respectively; the prevalence of moderate and severe

stenosis was generally 16.5% and 4%, which is lesser than those reported in the literature. In the studies by Masabani et al, Kiernan et al, and Waheed et al, the percentage of severe CtAD in CABG patients was reported as 6.2%, 7.7%, and 6.2%, respectively.^{9,10,15}

The prevalence of LtCA disease was associated with an age >65 years old ($P=0.002$), the status of unstable angina ($P=0.02$), and the presence of the proximal LCx stenosis ($P=0.03$); however, the severity of LtCA stenosis was in the statistical relationship with the presence of an occluded LAD ($P=0.013$), the proximal segment disease of LCx ($P=0.025$), and DM ($P=0.001$). The prevalence of RtCA disease was found to be statistically associated with an age >65 years old ($P=0.012$), and the presence of an occluded coronary artery ($P=0.009$) had a strong relationship with LAD occlusion ($P=0.017$) and the status of unstable angina ($P=0.02$). Conversely, the severity of RtCA stenosis was associated with age >65 years old ($P=0.01$) and DM ($P=0.001$). The latter data pointed out that age older than 65 years, the status of unstable angina, and proximal disease or occlusion of the left coronary branches are related to the prevalence of RtCA and LtCA diseases, while DM is the common factor to the stenosis severity of both diseases.

Strengths and Weaknesses of the Study

This study, which, to the best of our knowledge, is the first one to investigate the epidemiological aspects of CaAD in patients undergoing coronary artery transplantation in Chaharmahal and Bakhtiari province, can be valuable considering patients referred to a reference hospital in the province, the epidemiological face of this disease, and the characteristics of affected people in a suitable way, which can be highly useful and fruitful for health policy-makers. However, this study also had limitations in that the information about some important variables (e.g., height, weight, body mass index, and carotid souffle) has not been collected and analyzed for the patients. In addition, the information about the studied variables was collected cross-sectionally and simultaneously; as a result, causal inferences could not be made from the relationships observed in the study. Therefore, it is suggested that in future research, the relationships investigated in this study should be evaluated by considering a larger sample size and the structure of prospective cohort studies.

Conclusion

The prevalence of concomitant carotid disease in patients referred to CABG remains alarming and constitutes a hazard to perioperative stroke. The age older than 65 years, unstable angina status, and the presence of an occluded coronary artery are associated with CaAD. In addition, diabetes mellitus is associated with the severity of both left and right carotid artery stenosis. Further studies are mandated to investigate changes in the epidemiological features of the concomitant CtADs in the patients referred to CABG and on a larger scale for developing local

diagnostic and management guidelines.

Authors' Contribution**Conceptualization:** Mehran Dastanpoor, Arsalan Khaledifar.**Data curation:** Mathias Hossein Aazami, Elham Raeisi, Abdolmajid Taheri.**Formal analysis:** Mathias Hossein Aazami, Elham Raeisi.**Funding acquisition:** Arsalan Khaledifar.**Investigation:** Mehran Dastanpoor, Abdolmajid Taheri.**Methodology:** Mathias Hossein Aazami, Elham Raeisi.**Project administration:** Arsalan Khaledifar, Elham Raeisi.**Resources:** Mehran Dastanpoor, Arsalan Khaledifar, Mathias Hossein Aazami, Elham Raeisi, Abdolmajid Taheri.**Supervision:** Arsalan Khaledifar, Mathias Hossein Aazami.**Validation:** Arsalan Khaledifar, Mathias Hossein Aazami.**Visualization:** Arsalan Khaledifar, Elham Raeisi.**Writing—original draft:** Mehran Dastanpoor, Arsalan Khaledifar, Mathias Hossein Aazami, Elham Raeisi, Abdolmajid Taheri.**Writing—review and editing:** Arsalan Khaledifar, Mathias Hossein Aazami, Elham Raeisi.**Competing Interests**

The authors declared no conflict of interests.

Ethical Approval

This study was approved by the Ethics Committee of Shahrekord University of Medical Sciences (IR.SKUMS.REC.1398.223).

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